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The following specific examples are included as illustrative of the transdermal drug delivery systems and polymer matrices described herein. These example are in no way intended to limit the scope of the invention. Other aspects of the invention will be apparent to those skilled in the art to which the invention pertains.

## Example 1

A polymer matrix with the following composition is prepared:

Acrylic Adhesive	20%
Silicone Adhesive	56.9%
Povidone (PVP)	7.5%
Oleyl Alcohol	6.0%
Dipropylene Glycol, USP	8.0%
Estradiol	1.6%

(all % are % by weight based on the dry weight of the total polymer matrix)

The polymer matrix is applied to a release liner at a coat weight of 12.5 (●) or 15 (▲) mg/cm<sup>2</sup>.

Human cadaver skin permeation studies were performed to quantitatively determine the effective permeation through the stratum corneum. The stratum corneum was obtained from split thickness, cryo-preserved cadaver skin by the heat separation technique. Samples of 5/16" diameter were cut from the laminate, in quadruplicate, and mounted onto 1/2" cut pieces of the stratum corneum. These samples were then placed on modified Franz diffusion cells. The receptor was filled with 7.5 mL of 0.9% NaCl and 0.01% NaN<sub>3</sub> in deionized water. The cells were maintained at a constant 32° C. and were magnetically stirred at approximately 300 rpm. At specified time points, samples of the receptor phase were taken with complete replacement of the receptor phase. These samples were quantified by high-performance liquid chromatography (HPLC) utilizing Waters HPLC instrumentation. C-8 (15 cm×4.6 mm) 5 μm particle size columns (HYPERSIL made by MetaChem Technologies, Inc., Torrance, Calif.) were used at 50° C. (column temperature).

FIG. 1 illustrates the estradiol flux (μg/cm<sup>2</sup>/hr) over time (0-81 hours) from transdermal delivery systems according to the invention (▲ & ●), as compared to Vivelle-Dot® (◆).

The results show that the systems according to the invention have a greater flux than the Vivelle-Dot® product and are able to achieve therapeutic daily dosages despite their significantly smaller size.

What is claimed is:

1. A monolithic transdermal drug delivery system for estradiol, consisting of (i) a backing layer, (ii) a single adhesive polymer matrix layer defining an active surface area and, optionally, (iii) a release liner, wherein the single adhesive polymer matrix layer comprises an adhesive polymer matrix comprising estradiol as the only drug, wherein the adhesive polymer matrix layer has a coat weight of greater than about 10 mg/cm<sup>2</sup> and includes greater than

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0.156 mg/cm<sup>2</sup> estradiol, and the system achieves an estradiol flux of from about 0.0125 to about 0.05 mg/cm<sup>2</sup>/day, based on the active surface area.

2. The transdermal drug delivery system of claim 1, wherein the adhesive polymer matrix comprises a polymer blend comprising an acrylic adhesive, a silicone adhesive, and soluble PVP.

3. The transdermal drug delivery system of claim 1, wherein the adhesive polymer matrix comprises about 2-25% by weight acrylic adhesive, about 45-70% by weight silicone adhesive, about 2-25% by weight soluble PVP, about 5-15% penetration enhancer, and about 0.1-10% by weight estradiol, all based on the total dry weight of the adhesive polymer matrix.

4. The transdermal drug delivery system of claim 3, wherein the penetration enhancer comprises oleyl alcohol.

5. The transdermal drug delivery system of claim 3, wherein the penetration enhancer comprises dipropylene glycol.

6. The transdermal drug delivery system of claim 3, wherein the penetration enhancer comprises oleyl alcohol and dipropylene glycol.

7. The transdermal drug delivery system of claim 3, wherein the acrylic adhesive and silicone adhesive are present in a ratio of from about 1:2 to about 1:6, based on the total weight of the acrylic and silicone adhesives.

8. The transdermal drug delivery system of claim 1, wherein the adhesive polymer matrix comprises an amount of estradiol effective to deliver a therapeutically effective amount of estradiol over a period of time selected from the group consisting of at least 1 day, at least 2 days, at least 3 days, at least 4 days, at least 5 days, at least 6 days and at least 7 days.

9. The transdermal drug delivery system of claim 1, wherein the adhesive polymer matrix comprises an amount of estradiol effective to deliver an amount of estradiol selected from the group consisting of about 0.025, 0.0375, 0.05, 0.075 and 0.1 mg/day.

10. The transdermal drug delivery system of claim 1, wherein the system achieves an estradiol flux of about 0.0125 mg/cm<sup>2</sup>/day, based on the active surface area.

11. The transdermal drug delivery system of claim 1, wherein the system achieves an estradiol flux of about 0.0133 mg/cm<sup>2</sup>/day, based on the active surface area.

12. The transdermal drug delivery system of claim 1, wherein the system achieves an estradiol flux of about 0.015 mg/cm<sup>2</sup>/day, based on the active surface area.

13. The transdermal drug delivery system of claim 1, wherein the system achieves an estradiol flux of about 0.0167 mg/cm<sup>2</sup>/day, based on the active surface area.

14. The transdermal drug delivery system of claim 1, wherein the system achieves an estradiol flux of about 0.0175 mg/cm<sup>2</sup>/day, based on the active surface area.

15. The transdermal drug delivery system of claim 1, wherein the adhesive polymer matrix comprises about 1.6% by weight estradiol, based on the total dry weight of the adhesive polymer matrix.

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